Embolization as One Modality in a Combined Strategy for the Management of Cerebral Arteriovenous Malformations

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Summary

We attempted to assess clinical results of management of cerebral arteriovenous malformation using a combination of endovascular, surgical and radiotherapeutic approaches.

We retrospectively reviewed the angiographic and clinical data on prospectively collected consecutive patients treated by embolization from 1994 to 2004. The general philosophy was to attempt treatment by a combination of approaches only when an angiographic cure was likely or at least possible. The clinical outcome was assessed according to the modified Rankin scale.

Although 404 patients were collected, complete files and follow-ups are available for 227 or 56% only. Most patients presented with hemorrhages (53%) or seizures (23%). The final management consisted in embolization alone in 34%, embolization followed by surgery in 47%, embolization and radiotherapy in 16%, and embolization, surgery and radiotherapy in 3% of patients. The embolization procedure itself could lead to an angiographic cure in only 16% of patients. When the management strategy could be completed, the cure rate increased to 66%. Complications of embolization occurred in 22.6% of patients. Overall clinical outcome was excellent (Rankin 0) in 43%, good (Rankin 1) in 38%, fair (Rankin 2) in 10%, poor (Rankin 3-5) in 2%, and the death rate was 7%.

A combined strategy initially designed to provide angiographic cures cannot be completed in a significant number of patients; the total morbidity of treatment remains significant.

There is no scientific evidence that cerebral arteriovenous malformations should be treated, and no clinical trial to prove that one approach is better than the other. Various treatment protocols have been proposed on empirical grounds. Small lesions can often be eradicated, with surgery when lesions are superficial, or with radiation therapy for deeper ones. There has been little controversy regarding therapeutic indications in these patients [1]. The management of larger AVMs, sometimes in more eloquent locations, is much more difficult and controversial [2-4]. Endovascular approaches have initially been developed to meet this challenge [5,6]. It became quickly evident that embolization alone would rarely suffice to completely cure these lesions. The philosophy behind combined approaches is founded on 2 opinions: 1) There is no proven value of partial embolization, not even "partial benefits", and treatment should aim at an angiographic cure [7] and 2) By appropriately tailoring all available tools to each situation, such a cure could be reached with minimum or reasonable risks.

We have used such a combined strategy for more than a decade now. Endovascular techniques and materials have evolved, and it is perhaps possible today to reach a cure by emboliza-

tion alone in a larger proportion of patients than before[8]*. Aggressive embolizations, aiming for an endovascular cure, even sometimes in large lesions, have recently been promoted for their power or criticized for their risks*[9]*. But before evaluating the advantages and inconveniences of new treatments, it may be wise to review the results we could achieve with a conventional approach combining endovascular, surgical and radiotherapeutic techniques.*

Patients and Methods

Treatment Strategies

From January 1994 to December 2004, all patients with cerebral arteriovenous malformations referred to endovascular treatment in our service were prospectively entered in a computerized database. All patients were evaluated by a multidisciplinary team to reach a group consensus regarding indications for treatment and to determine the best management strategy. The general philosophy was to offer treatment of the AVM only when an angiographic cure was felt to be possible by one approach or another (or by a combination of treatment), and the risk/ benefit balance was felt to be favorable; hemorrhagic presentations were usually considered stronger indications, and treatment considered a priori more beneficial in patients younger than 50. Surgery alone was favored for small superficial lesions, radiotherapy for small deep lesions (<10 cm^3), except for those in the brain stem or close to the optic nerve, chiasm or radiations. Surgery was usually preceded by embolization when the lesion was large or fed by less accessible feeders such as deep perforators. Radiation therapy was preceded by embolization in the presence of a macroscopic fistulae or of an angiographic risk factor after hemorrhage, such as a nidal aneurysm.

Because an angiographic cure using embolization alone was considered an unlikely outcome, it was rarely used in patients in whom surgery or radiation therapy were excluded. Exceptions included 1) patients presenting with hemorrhage and with an identified angiographic risk factor that could be selectively targeted for embolization[10,11] and 2) rare patients with progressive deficits and presumptive evidence of congestive venopathy. In certain patients only selective treatment of associated berry aneurysms on the circle of Willis, usually with platinum coils, was offered.

Endovascular Treatment

Endovascular techniques have progressed during the decade that is the object of this study, but some general features can be recognized: All patients were electively treated under general anesthesia, using a femoral approach, under systemic anticoagulation with heparin. Urgent treatment was performed exceptionally, in patients with aneurismal hemorrhages, and focused on the berry aneurysm thought to be causal, or on arterial or nidal aneurysms or false aneurysms, especially in rare cases of early rebleeding. Embolization was usually staged into a number of sessions to be determined according to interim results. Only flow guided catheters were used during most of the 90's (usually Magic (Balt) or Spinnakers (Target Therapeutic)), over-the-wire catheters in the 2000's (usually Ultraflow, MTI). The goal of embolization was to reach the nidus with a liquid agent, whether the embolization was preoperative or pre-radiotherapeutic. The embolic agent was virtually always n-butyl-2-cyanoacrylate mixed with a lipidic contrast agent (Lipiodol; Guerbet), in varying concentrations, most commonly 33% in the early years, 18-20% in the later years, except for large high-flow fistulae. The feeder bearing a risk factor was usually attacked first. Otherwise the procedure was usually performed from the largest to the smaller feeders. Ethylene vinyl alcohol was only recently and occasionally used. We relied on angiographic anatomy, never on functional testing, before injecting the embolic mixture. Embolization was not meant to reach the draining veins in most cases. Final angiograms were used to qualify in a semi-quantitative manner the efficacy of the procedure (less than 1/3; 1/3-2/3; more than 2/3 of the nidus eradicated), and to look for venous outflow restrictions. Only when venous blood flow was stagnating were patients occasionally covered with heparin for another 24 hours. We did not systematically use hypotension after embolization. Patients were kept in the intensive care unit for 24 hours and discharged no earlier than 2 days after the procedure. All patients were studied by CT the next day to detect asymptomatic complications. An angiographic cure was defined as the absence of any residual nidus or early draining vein on 2 complete catheter angiograms, at least 3 months apart.

Surgery and Radiation Therapy

Resection of AVMs was accomplished in one stage by standard methods under microscopic

guidance, taking care to completely dissect the plane between the nidus and the normal brain, coagulating or clipping all arterial feeders before an attempt at ligating draining veins. Follow-up CT scans to document potential complications were always performed 24 hours later. A postoperative angiogram, even when it showed complete resection, was confirmed by a follow-up angiogram 3 months later.

Radiation therapy was never performed after embolization or surgery without a 3-month follow-up catheter angiogram, to minimize risks of miss-targeting lesions or portions of lesions that would only be temporarily occluded. Radiation therapy was delivered under stereotactic angiography guidance using multiple arcs LINAC (Radionics). A catheter angiogram was scheduled 2 years after radiation therapy, and yearly thereafter if the obliteration was incomplete.

Data Collection

The clinical charts and radiographic documents of prospectively entered patients were retrospectively studied to collect the data concerning: age, sex, clinical presentation, treatment strategies, complications, length of follow-up, and angiographic outcome. This report is preliminary and many clinical and radiographic factors remain to be studied. Our goal was to give an overall portrait of global results. The long-term clinical outcome was determined by telephone interviews according to the modified Rankin scale.

Results

A total of 404 patients with AVMs were entered into the database. Patients treated for berry aneurysms in whom the AVM was left untreated were excluded (23 or 6%). Complete files have been recovered, examined and follow-up interviews have been completed for 227 patients (56%) that form the basis of this preliminary report. There were 124 women and 103 men. The mean age was 43.6 years.

Most patients presented with hemorrhage (53%) or seizures (23%); some had focal neurological deficits (5%); some patients presented with headaches only (8%) or were completely asymptomatic (5%).

The treatment was considered final in 204 or 90% of these patients with complete files. The management finally ended up in embolization alone in 70 or 34%, embolization followed by surgery in 96 or 47%, embolization and radiotherapy in 32 or 16%, and embolization, surgery and radiotherapy in 6 or 3% of patients.

The endovascular procedure was able to obliterate less than 1/3 of the lesion in 19% of cases, between 1 and 2/3 in 30%, more than 2/3 of the lesion in 36%, and could lead to an angiographic cure in 16% of patients.

Complications occurred in a total of 46 or 22,6% of patients. Most frequent complications were hemorrhagic (35 or 17%) but 10 were infarcts (or 5% of patients). Not all technical complications were clinically eloquent, but endovascular treatment was responsible for 3 deaths. Perforations occurred only with over-the-wire catheters, but were infrequently symptomatic. Hemorrhages related to microcatheter retrieval were less frequently of consequence, while most severe hemorrhages, necessitating urgent surgery or leading to mortality occurred in a delayed fashion, most often during the following hours, presumably from venous occlusions and rupture of the AVM. Other events occurred after additional treatment: 9 permanent complications from surgery and 3 from radiation therapy should be added. The technical complications and clinical consequences of complications have not yet been correlated for the various procedures, and the morbidity related to the initial hemorrhage has not been determined. Thus it is not currently possible to attribute a poor clinical outcome to one modality or the other, or to the presenting event. The mean clinical follow-up was 32 months. Overall clinical outcome was excellent (Rankin 0) in 43%, good (Rankin 1) in 38%, fair (Rankin 2) in 10%, poor (Rankin 3-6) in 9%, including a death rate of 7%.

A combined approach (embolization plus surgery or radiotherapy or both) led to a proven angiographic cure in 66% of patients in whom it could be completed.

Discussion

Cerebral AVMs come in a wide array of clinical presentations, size, location, and architecture. Available treatments are also widely different in nature, power, and risks, and a "combined approach" encompasses many different combinations in different orders. In this context, generalizations are almost impossible. Predictions based on series, however reliable in the

aggregate, are notoriously uncertain at the individual level. Thus a casuistic approach would seem appropriate. But then how is knowledge possible? On what principle should we found our actions?

There is very little science in the management of cerebral AVMs and most actions are based on opinions. The management of AVMs is decided subjectively, literally, on a case-by-case basis, using clinical judgment. True rational decisions would follow an accurate estimate of the balance between the risks of the disease versus risks/benefits of treatment. Unfortunately the natural history of untreated AVMs remains unknown, and risks of treatment using different approaches are poorly documented, most often with published case series from single institutions that are by definition biased for best results.

All natural history data available and all information on treatment modalities are grade C evidence [12, 13]. The lifetime risk of hemorrhage has been estimated as 105 minus patient's age in years [14], the annual risk between 2 and 4%, and there may be a higher risk during the first year following an initial hemorrage (7 versus 3%) [11,13,14]. Large deep lesions may be at higher risk [15]. Our knowledge regarding risks of treatment is also quite weak; the yearly risk of neurological events after radiation therapy has been quoted at 3,9% [16]; risks of surgical resection depend on the type of lesion; when classified according to the Spetzler-Martin classification, risks have been estimated at 2-14% with grades I and II, 25-50% with grades IV and V [17-20]. Risks of endovascular treatment, often quoted as 14% (2% disabling) with 1% deaths, have been said to vary according to patient's age, deficit at presentation, and number of sessions [21,22]. The complication rate that we quote needs confirmation: a bias of this work is the uncertainty of the denominator; only 56% of patients were included and files are more likely to be completed in complicated cases. Benefits of partial embolization are controversial [4,23].

To provide a more consistent, rational consultation and minimize extraneous factors such as the "as good as the last case" phenomenon, we attempted to reach a multidisciplinary consensus on all management decisions during formal weekly rounds. Nevertheless the process depends on a recollection of past experiences, most frequently biased, on intuition, and on an "objective" estimate of particular risks and "honest" assessment of individual skills. Unfortunately the dangers of trying to duplicate published successes as well as the pitfall of "wishful thinking" in a case-by-case, step-by-step decision process is ever-present, even in this context. An essential requirement to the credibility of this casuistic approach would be to assure a feedback mechanism, such as systematic critical review of management results at regular intervals.

There are a number of assumptions that are intrinsic to the management of AVMs using a combined approach: the goal is to reach an angiographic cure but no one has ever shown that such a result was associated with an improved long-term outcome; conversely we and others have seen patients that had been qualified as cured, only to present later on with hemorrhages [24]. Thus we now insist on 2 normal angiograms at a 3 month-interval before calling a cure.

Many neurosurgeons feel that preoperative embolization is helpful; it may diminish blood loss, permit an easier dissection of the nidus, which is often better delineated, and perhaps it effectively replaces the surgical staging that was once proposed to decrease operative complications with large lesions. But these statements are opinions that are not shared by all surgeons, and one should remember that, while embolization may decrease the risk of surgery, it carries risks of its own, especially when multiple sessions are necessary [22,25].

Another assumption is that embolization improves the potential efficacy of radiation therapy by decreasing the total volume of lesion that needs to be treated, or by decreasing flow within the lesion. We have found the reliable prediction of the results of pre-radiotherapeutic embolizations a tricky task, especially in large lesions.

While an overall reduction in flow is often spectacular, a true concentric reduction of size to the theoretical 10 cm^3 limit is often difficult to reach. The final outcome of radiation therapy is not always captured by the follow-up period, although we know that patients treated by radiation may have delayed complications [26] and a persistent incidence of hemorrage [27]: in a recently published series of patients treated by radiotherapy, preceded by embolization in most cases, the annual neurological event rate did not differ from the estimated natural history [16].

Finally an accurate estimate of risks in-

volved, before selective endovascular exploration, and without knowledge of the number of sessions that ultimately will be necessary to bring the lesion to surgery or radiotherapy, is almost impossible. Thus, even in a multidisciplinary context, the a priori evaluation of our capacities to reach a cure, and the risks undertaken to reach that goal, are more often in the order of wishful thinking than we would like to believe.

Our results show there is room for improvement. Recently proposed attempts at aggressive embolization as a single treatment modality should be critically assessed but in the light of the results we can so far achieve.

In depth study of our population may allow the identification of features pertinent to the outcome, such as size or grade of the lesion. We believe that the improved management of brain AVMs needs collegial efforts to define, systematize, classify lesions, and hopefully standardize treatment strategies in prospective trials to bring some science into this field [28, 29].

Conclusion

Although our aim was to provide a combination of approaches to maximize the chances of an angiographic cure and minimize risks on a case-by-case basis, the management-related morbidity was significant while the success rate remained below expectations.

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